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EXAMINER	
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1638	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/978,274	THOMAS ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-55,57 and 59-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-55,57 and 59-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/25/08 has been entered.

Claims 46-55, 57, and 59-71 are pending and are examined.

Claim Objections

At claim 52, it is suggested that "SEQ.ID.NO.:2 be changed to ---SEQ ID NO: 2--, for formality.

New Matter Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 71 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims is drawn to a method of inducing cell death in specific cells of a plant comprising exposing said plant comprising a chimeric gene comprising a nucleic acid encoding pokeweed antiviral protein under the control of an inducible promoter, wherein the protein is at least 90% to 95% homologous to SEQ ID NO: 2, 6 or 8. However, support for the limitation "90% to 95%" cannot be found in specification or in the claims as originally filed. Therefore, the limitation is considered to be new matter. Therefore, Applicant is requested to point to support for the limitation in the originally filed application or to delete the NEW MATTER in response to this rejection.

Claim Rejections - 35 USC § 112

Claims 46-51, 53-55, 57, 59-63, 66-69, and 70-71 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing cell death in specific cells in specific plant species by introducing a chimeric gene comprising a nucleic acid sequence encoding the pokeweed antiviral protein (PAP) of SEQ ID NO: 2, 4, 6 or 8, does not reasonably provide enablement for a method of inducing cell death in any plants using sequences having less than 100% sequence identity to the disclosed sequences. This rejection is repeated for the reasons of record as set forth in the last Office action of 03/25/08. Applicant's arguments filed 08/25/08 have been fully considered but are not deemed persuasive.

The claims are drawn to, inter alia, a method of inducing cell death in specific cells of a plant, said method comprising exposing a plant comprising a chimeric gene comprising a nucleic acid encoding pokeweed antiviral protein that is at least 70%, 80 or at least 90% to 95% homologous to SEQ ID NO: 2, SEQ ID NO: 6, or SEQ ID NO: 8

operably linked to pathogen or chemical inducible promoter, wherein the expression of said pokeweed antiviral protein induces cell death in said specific cells. The claims are also drawn to said method wherein the nucleic acid hybridizes under stringent conditions to SEQ ID NO: 1, 3, 5 or 7 and encodes functional PAP.

Applicant teaches constructs containing a nucleic acid sequence encoding SEQ ID NO: 2, 4, 6, or 8 under the control of 35S CaM or a nematode inducible promoter for transient assay in tobacco protoplasts to show PAP-S mediated ribosome inactivation (Figures 5-7). Applicant also teaches transformation of tobacco and potato plants with said constructs and expression of Pro-PAP-S or mature PAP-S in nematode infected root cells. Applicant teaches that the transformation of tobacco with SEQ ID NO: 1 encoding pro PAP-S and potato with a nucleic acid encoding the mature PAP-S or Pro-PAP-S sequences resulted in transgenic tobacco and potato plants with nematode resistance (Figures 13-14). Applicant teaches that transformation of tobacco cells with a nucleic acid encoding mature PAP-S (SEQ ID NO: 4) repeatedly failed to produce transformed tobacco showing that the mature PAP-S sequence does not function in tobacco plants.

Applicant does not provide guidance for a method of inducing cell death using nucleic acids other than SEQ ID NO: 1, 3, 5 or 7. Applicant does not teach that nucleic acids encoding the antiviral viral proteins of SEQ ID NO: 2, 4, 6 or 8 can induce cell death in specific cells in all and any plant species using exemplified or non-exemplified pokeweed encoding nucleic acids. Neither the instant specification nor the prior art provide evidence that pokeweed antiviral proteins can function in any plant species.

Nielson et al (Annu. Rev. Plant Physiol. Plant Mol. Biol. (2001), vol. 52, pp. 785-816, in record) teach about ribosome inactivating proteins including pokeweed, their enzymatic activities, and their complex biological role. Nielson et al specifically states that while plant RIPs have been linked to antiviral, antifungal and insecticidal activity in transgenic plants, the mechanism of these effects remains unresolved (see at least the Abstract on page 785). At the paragraph bridging pages 801 and 802, the cited reference states "(a)lthough the enzymatic mechanism of RIP activity is well defined, the physiological steps by which ribosome inactivation leads to cell death are not well understood".

The prior art teaches that transformation of a plant with a PAP encoding nucleic acids is highly unpredictable. For example, Lodge et al (PNAS, vol. 90, pp.7089-7093, 1993, Applicant's IDS) teach that the expression of PAP in transgenic plants may result undesired phenotype such as stunted, molted and sterility in the plant. Lodge et al teaches that tobacco plants expressing high levels (above 10ng/mg of protein) of wild type and mutant PAP tend to have stunted and mottled phenotype, and some the plants were sterile (see page 7090, Results and Discussion). On the other hand, Barbieri et al (Biochemica et Biophysica Acta, vol. 1154, pp. 237-282, 1993, Applicant's IDS) teaches that plant RIPs including PAP can act on their ribosome only at high levels of concentrations (see pages 251-252, section III-A).

In addition, the working examples disclosed in the specification are limited to the use of unmodified nucleic acids encoding pro-PAP-S (SEQ ID NO: 2), mature PAP-S (SEQ ID NO: 4), PAP-S α (SEQ ID NO: 6), and PAP-Sβ (SEQ ID NO: 8) in potato and

tobacco. The ability of pro-PAP-S, PAP-S α and PAP-S β in tobacco and potato, and SEQ ID NO: 3-4 in potato to induce cell death in specific cells cannot be extrapolated to all nucleic acid that hybridize to SEQ ID NO:1, 3, 5 or 7 or encoding a PAP having at least 70%, 80% or 9o to 95% to SEQ ID NO: 2, 6 or 8, absent further guidance.

Therefore, given the breadth of the claims, the state of the prior art; the nature of the invention; the limited working examples, and the unpredictability with respect to PAP activity in transgenic plants as discussed above, the claimed invention is not enabled throughout the broad scope. See In re Wands 858 F.2d 731, 8USPQ2nd 1400 (Fed. Cir, 1988).

Response to Arguments

Applicant argues that one of skilled in the art can practice the full scope of the claimed invention because Applicant asserts that at the time this application was filed it was known o one of skilled in the art which amino acids in a PAP are essential for the induction of cell death in a transformed plant. Applicant cites Chaddock J.A. et al (Nucleic Acids Res 22(9) 1536-1540 (1994) to support this position. Applicant asserts that Chaddock et al provide examples of pro-PAP mutations in the amino acid residues that are essential for ribosome inactivating ability. Applicant, therefore, asserts that since the amino acid sequence of PAPs are very similar, one skilled in the art would know which amino acid residues in SEQ ID NO: 2, 6, or 8 can be modified while retaining the ribosome inactivating ability of the protein. Applicant further asserts that the specification provides guidance for assays to test whether a given amino acid sequence has the ability to induce cell death. Applicant, therefore, submits the claimed

invention is enabled throughout the broad scope. Applicant requests that the rejection be withdrawn.

These arguments have been fully considered but are not deemed persuasive for the following reasons: firstly, Chaddock et al teach PAP mutations in the amino acid residues that are essential for ribosome inactivating ability in a prokaryotic. Chaddock et states "mutation R68G led to a protein that appeared to be inactive towards prokaryotic ribosomes, but also very poorly active towards eukaryotic ribosomes. This mutation is currently under further investigation." Chaddock et al do not teach amino acid residues or regions in a PAP that are essential for the induction of cell death in a transformed plant. Secondly, Applicant provides no evidence that shows PAP amino acid sequence are very similar and have the same effect in prokaryotic and in plants. In fact, both the prior art (as discussed above in the scope of enablement rejection) and Applicant's own specification (working examples) show that PAPs function differently even between different plant species. Thirdly, since Applicant has not provided a copy of the cited reference, Examiner has relied upon the abstract only to evaluate the teaching of the reference. Fourthly, the rejected are drawn to a method of inducing death cell in specific plant cells of any species using modified PAP nucleotide sequences rather than methods of testing whether a given amino acid sequence can induce cell death in a plant.

In Genentech Inc. v. Novo NordiskAIS (42 USPQ2d 1001 at p. 1005) The CAFC stated "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not workable...While every

aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry outthe invention...[W]hen there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required ....It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". Id. In this case, as in Genentech, the specification does not provide the "reasonable detail ..... to enable members of the public to understand and carry out the invention" as broadly claimed.

Therefore, for all the reasons discussed above and in the last Office actions, the claimed invention is not enabling throughout the broad scope. Therefore, the rejection is proper.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 46-55, 57, and 59-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Tumer et al (WO 99/60843, Applicant's IDS) and Kanieswski et al (6, 015, 940 in view of Thomas et al (US 6,140,554) and Poyet et al (FEBS (1997) vol 409 no.1-2, pp. 97-100).

The claims are drawn a method of inducing cell death in specific cells of plants including potato, said method comprising exposing a plant comprising a chimaeric gene comprising a nucleic acid molecule encoding a pokeweed antiviral protein having 70%, 80%, or 90% to 95% sequence identity to SEQ ID NO: 2, 4 or 6, and an inducible promoter which induces expression of said protein in said specific cells, upon exposing said plant to a pathogen or chemical or which is cell type specific, wherein the expression of said PAP induces cell death in said specific cells of said plant. The claims are also drawn said method, wherein the nucleic acid is either SEQ ID NO: 1, 3, 5, 7, or encodes SEQ ID NO: 2, 6 or 8 or that hybridizes thereto under specified hybridization conditions and encodes a proPAP-S or a C-terminal deletion thereof, or encodes a mature PAP-S, PAP-Sά or PAP-S ß that induces cell death in specific cells of the plant.

Tumer et al teach a method of producing transgenic plants expressing a chimeric gene comprising a nucleic acid encoding pokeweed antiviral protein designated as PAP

II, including full length, wild type and a truncated protein PAP II with deleted C-terminal, operably linked to a promoter expressible in plant cells; said promoter can be a pathogen inducible or tissue-specific for expression of said promoter in tissue-special manner or inducible by a pathogen. Transgenic plants expressing pokeweed antiviral protein having viral and fungal resistance are also disclosed (pages 16-23). The cited reference also teaches that the nucleic acids encoding PAPII can be used to induce nematode resistance using in a transgenic plant (page 9, 1st full paragraph). The cited reference further teaches different promoters that can be used to express PAP in transgenic plants and their availability in the prior art; promoters include wound-induced, specific cell types (such as leaf epidermal cells, mesophyll cells, root cortex cells), specific tissues or organs types (roots, leaves or flowers, for example); light-induced or other temporally-regulated promoter, or chemically regulated promoters.

Kanieswski et al teach a method of inducing viral resistance in tobacco and potato plants and plant cells, the method comprising transforming said plants/plant cells with a chimeric gene comprising a DNA sequence encoding PAP' or a mutant thereof retaining PAP activity, a tissue-specific or inducible promoter, N-terminal signal sequence capable of targeting said PAP' in specific cells of the plant. The reference further teaches transgenic potato plants that are resistant to PVX, PVY and PLRV (potato virus X, Y, and potato leafroll viruses) (column 2; column 9, lines 24-41; Examples 2-3; and columns 27-28). In column 3, lines 2-10 and column 4, lines 3-30, Kanieswski suggests that other forms of PAP including PAP-S and PAP-II can be isolated from pokeweed seed and summer leaf, respectively, and used in the disclosed

method. In column 9, lines 25-45, the cited reference suggests expressing the pokeweed antiviral protein in a tissue-specific manner in cells where viral infection is known to occur.

Each of Tumer et al and Kanieswski et al do not explicitly teach a cell-specific pathogen inducible promoter.

Thomas et al teach methods of producing nematode resistant transgenic plants using cell-specific promoters such as KNT1 and RB7. At the paragraph bridging columns 4 and 5, Thomas et al teach the importance of using feeding cell-specific promoters with cell-death system to disrupt the nematode feeding cells.

Tumer et al and Kanieswski et al in view of Thomas et al do not explicitly teach PAP-S nucleic acids of SEQ ID NO: 1, 3, 5 or 7 or encoding SEQ ID NO: 2, 4, 6, or 8.

Poyet et al teach the isolated nucleic acids of SEQ ID NO: 1, 3, 5 or 7 encoding the PAP SEQ ID NO: 2, 4, 6, 8 PAP-S activity.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of transforming a plant with a pokeweed antiviral protein encoding DNA to induce viral or fugal resistance as taught by Tumer et al, and to modify that method by incorporating any of the cell-specific and pathogen inducible promoters known in the prior art such as KNT1 or RB7 taught by Thomas et al to induce cell death in specific cells of the plant, without any unexpected results. One would have been motivated to use any of the PAPs known in the prior taught by either Tumer et al, Kanieswski et al or Poyet etal, given the phytotoxic, antiviral, and antifungal disease resistance activity of PAPs in transgenic plants as taught by each of Tumer et

al, Kanieswski et al or Poyet etal, and its antinematode activity as suggested by Tumer et al. One would have been motivated to use cell-specific inducible promoters such as KNT1 or RB7 given that they are well characterized and have been successful used in construct to induce cell death in transgenic plants as taught by Thomas et al, and given the problem of plant cell/organ specific pathogens such as nematodes that infect only roots as suggested by Thomas et al and as known to one of ordinary skill in the art. Therefore, the claimed invention as whole was clearly a *prima facie* obvious.

Remarks

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571)272-0797. The examiner can normally be reached on M-TH 8:00 am to 5:30 PM, and every other Friday from 8:00 AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MAI
11/10/2008

/Medina A Ibrahim/
Primary Examiner, Art Unit 1638